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Cancer Incidence in Atomic Bomb Survivors. Part 1: Use of the Tumor Registries in Hiroshima and Nagasaki for Incidence Studies

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More than 30 years ago, population-based tumor registries were established in Hiroshima and Nagasaki. This report, the first of a series of papers on cancer incidence, describes methodological aspects of the tumor registries and discusses issues of data quality in the context of the Life Span Study (LSS) cohort, the major atomic bomb survivor population. The tumor registries in Hiroshima and Nagasaki are characterized by active case ascertainment based on abstraction of medical records at area hospitals. augmented by tissue registries operational in the area and a number of clinical and pathological programs undertaken over the years among the atomic bomb survivors. Using conventional measures of quality. the Hiroshima and Nagasaki tumor registries have a death certificate-only (DCO) rate of less than 9%, a mortality/incidence (M/I) ratio of about 50%, and a histological verification (HV) rate in excess of 70%, which place these registries among the best in Japan and comparable to many established registries worldwide. All tumor registry data pertaining to the LSS population were assembled, reviewed and handled with special attention given to the quality and uniformity of data based on standardized procedures. Special studies and monitoring programs were also introduced to evaluate the quality of the tumor incidence data in the LSS. Analyses were performed to examine the quality of incidence data overall and across various substrata used for risk assessment such as age, time and radiation dose groups. No significant associations were found between radiation dose and data quality as measured by various indices. These findings warrant the use of the present tumor registry-based data for studies of cancer incidence in the atomic bomb survivors.

INTRODUCTION

Cancer is a major health effect of exposure to ionizing radiation. Until now, the Radiation Effects Research Foundation (RERF)[1] has relied mostly on mortality data in assessing cancer risk associated with exposure to the atomic bomb. Recently, comprehensive data on cancer incidence became available. The data on cancer incidence offer several advantages over data on mortality. Detailed medical data obtained from hospital records provide information needed for accurate and specific diagnosis. Such information is not generally available from studies based on death certificates, and errors in death certificate diagnoses can occur *(1,2)*. A more precise appraisal of the time of disease onset for incident cases also allows for a better evaluation of temporal patterns of cancer. Furthermore, incidence studies enable the comprehensible ascertainment of cancers with a favorable pognosis (e.g., breast, thyroid and skin).

Tumor registries are essential to the systematic collection. management and analysis of incidence data for a population. More than 30 years ago, population-based tumor registries were established in Hiroshima and Nagasaki. These were among the first tumor registries in Japan. The objectives of these registries were twofold: the collection and management of cancer data in the community and the use of these data for the assessment of cancer risks-associated with radia-

[1] Abbreviations used: ABCC, Atomic Bomb Casualty Commission: ATB, at the time of the bombing: DCO, death certificate only: HV, histological verification: IARC, International Agency for Research on Cancer: ICD-O, lnternational Classification of Diseases for Oncology: LSS, Life Span Study: M/I, mortality/incidence ratio: NIC, not in city: NOS. not otherwise specified: RERF, Radiation Effects Research Foundation: SEER, Surveillance, Epidemiology and End Results.

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tion from the atomic bomb. Data from the tumor registries pertaining to both the general population and atomic bomb survivors were reported for the first few years of their operation *(3–5)*. Subsequently. delays in data collection from certain hospitals led to uncertainties regarding the completeness of case ascertainment. Thus few reports on total cancer incidence based on the population-based registries have been published and their data have been used mainly for studies of specific cancer sites including thyroid *(6)*, breast *(7)*, lung *(8*, 9), stomach (10), colon. rectum *(11)* and ovary *(12)* among the atomic bomb survivors. The last tumor registry report for the Life Span Study (LSS) was limited to the analvsis of data for the Nagasaki portion of the cohort for the years 1959–1978 *(13)*.

Over the past several years, improvements have been made in the data collection and management systems of the tumor registries. With the close inspection and revision of all earlier data. high-quality data on cancer incidence for the LSS cohort since the outset of the registry in each city are now available. This report. the first of a series of papers on cancer incidence in the LSS, describes the history of the tumor registries as well as current methods of data collection and quality control. The usefulness of risk estimates based on incidence is dependent on the quality of the data on which they are based. Parts II, III and IV of the series provide a detailed evaluation of the incidence of solid tumors *(14)* and hematopoietic and lymphatic malignancies *(15)*. and a comparison of incidence and mortality data *(16)*.

TABLE I

Major Characteristics of Tumor and Tissue Registries, Hiroshima and Nagasaki

Case-finding and data acquisition methods	1. Hospital record abstraction 2. Supplemented by notification and mortality information	1. Hospital record abstraction 2. Supplemented by notification and mortality information	1. Hospital record abstraction 2. Voluntary notification 3. Supplemented by mortality information	1. Visits to hospitals and pathology laboratories 2. Storage of pathology slides	1. Visits to hospitals and pathology laboratories 2. Storage of pathology slides	1. Hiroshima and Nagasaki City Tumor Registries 2. Hiroshima and Nagasaki Tissue Registries 3. Nagasaki Prefectural Registry 4. Leukemia Registry 5. Mortality search 6. RERF records 7. RERF special studies

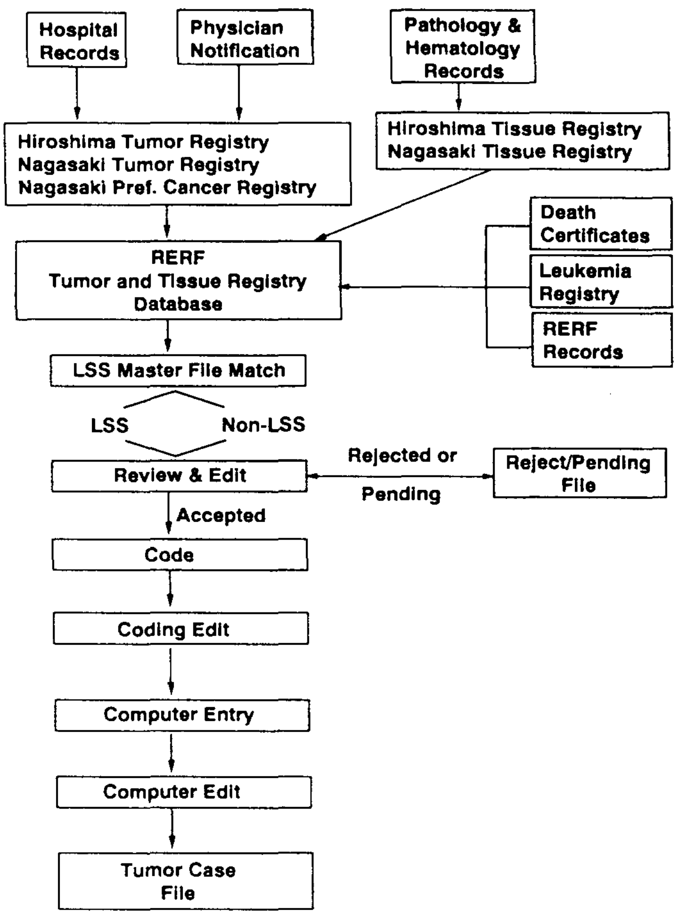

FIG. 1. Data flow and linkage process in RERF tumor and tissue registry database.

HISTORY AND ORGANIZATION OF TUMOR REGISTRIES

Hiroshima and Nagasaki Tumor Registries

Agreements between the Atomic Bomb Casualty Commission (ABCC) and the city medical associations to establish population-based city tumor registries were concluded in 1957 in the city of Hiroshima and in the following year in the citv of Nagasaki (Table I). The Hiroshima and Nagasaki medical associations each established a committee to oversee the registries, while ABCC, and later RERF, was responsible for the day-to-day operations including data collection. management and statistical analysis (5). The medical associations in each city have continually provided administrative support to the registries to assure the collaboration of participating hospitals.

Reports on tumor incidence in the atomic bomb survivor cohort. as well as in the general populations of the cities of Hiroshima and Nagasaki *(3–7).* were published several years after the start of the registries. Analyses of the data for 1957-1959 showed that about 58% of the cases registered in Hiroshima had cancer which had been diagnosed histologically. Also, 94% of cancers diagnosed clinically were confirmed by ABCC autopsy data, while 76% of the autopsied cancers had been diagnosed clinically as such *(3).* The tumor registries became less active in subsequent years, especially in Hiroshima. mainly due to problems in sustaining collaboration with several of the large hospitals. Population-based incidence data for Nagasaki were published in *Cancer Incidence in Five Continents* for 1973 through 1982 *(17,18),* but comparable data for Hiroshima were published only for 1978-1980 *(18).* Due to improved collaborative relationships and concentrated efforts undertaken by RERF in recent years. problems in data collection in Hiroshima were resolved and reportable cases were identified retroactively. Currently. ascertainment of newly diagnosed tumor cases is undertaken routinely in both Hiroshima and Nagasaki. Intense efforts are being made by both registries to ensure data quality similar to that required in the Surveillance. Epidemiology and End Results (SEER) program in the United States *(19).* As a result, data for cancer incidence in both Hiroshima and Nagasaki were included in the latest volume of *Cancer Incidence in Five Continents (20).*

LSS Tumor Registry

Tumor patients from Hiroshima and Nagasaki Prefectures who are part of the LSS cohort are included in a subset of the tumor registry database, referred to as the LSS Tumor Registry *(21).* This registry was established in 1988, but data from 1958 on were entered retroactively. The LSS Registry is managed together with the general Hiroshima and Nagasaki Tumor Registries. As discussed below, the LSS Tumor Registry ascetains incident cases from a variety of prefectural data sources. and thus its catchment area is the entire prefecture in both Hiroshima and Nagasaki.

To identify individuals in the LSS sample. all patients accessed through the Hiroshima and Nagasaki Tumor and Tissue Registries. as well as the Nagasaki Prefectural Cancer Registry, are matched against the RERF Master File database (Fig. 1). Matching is based on personal identification data including full name. date of birth (or age), sex and residence, using a computer algorithm supplemented by manual verification. Curre ntly, about 8% of newly diagnosed tumor cases reported to the city tumor registries are identified as members of the LSS (Table I).

For the LSS Registry, there arc additional sources of case ascertainment and medical data. For many years. ABCC/RERF has undertaken major research programs targeted at both the atomic bomb survivors and residents in the community. Among these. the Autopsy and Surgical Pathology Program. the Adult Health Study Program and a series of site-specific cancer studies serve as the additional sources for the ascertainment of tumor cases among the members of the LSS sample. Data from these sources were incorporated into the

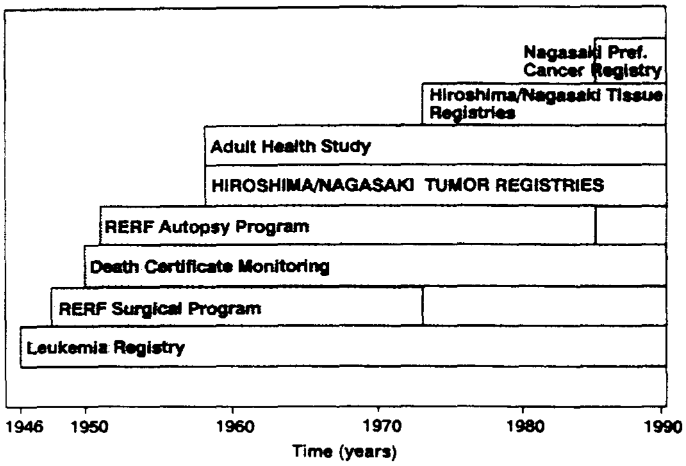

FIG. 2. Tumor ascertainment methods for LSS cancer incidence studies and their time coverage.

registry database. Figure 2 illustrates each source used for case ascertainment and the years covered by each. The availability of multiple sources is evident for most of the years.

In reconstructing the LSS tumor registry database, special efforts were made to ensure that all eligible cases from various sources are ascertained and that data with variable quality and quantity from multiple sources are managed in uniform fashion. To standardize diagnostic criteria and procedures for handling data. registry staff reviewed all documents for LSS tumor patients accessed since 1958. The documents reviewed included not only tumor registry records but also tissue registry records. autopsy protocols. surgical pathology reports. AHS medical charts and records from previous site-specific cancer studies. For cases with inadequate information. hospitals were revisited and hospital records were reviewed once again. After all the records were reviewed. data were entered into a newly developed database system and various data quality assurance measures including intensive logical checks were implemented. The report on the incidence of solid tumors in the LSS cohort and the companion papers are based on the LSS tumor registry data. which are

METHODS OF CASE ASCERTAINMENT

The tumor registries in Hiroshima and Nagasaki employ identical methods of tumor registration. The registries ascertain the majority of cases by searching hospital records actively for mention of cancer or cancer-related diagnoses. Case-finding is also supplemented by data obtained from the Hiroshima and Nagasaki Tissue Registries, the Nagasaki Prefectural Cancer Registry and the Leukemia Registry, notification by physicians and death certificates (Fig. 1). Currently, reportable diagnoses include all malignant and *in situ* neoplasms, as well as benign tumors of the brain and central nervous system, pineal glands and pituitary, corresponding to ICD-O topography codes 140-199 and behavior codes 2 and 3 plus ICD-O codes 191, 192 and 194 with behavior code 0 *(25).* Until 1980, other selected benign tumors including those of the salivary glands. colon and stomach were also reportable.

Hospital Record Abstraction

This is the most important form of case ascertainment employed by the tumor registries in the two cities, and more than 70% of registered cases are accessed by this method. Case-finding and data collection are carried out by trained RERF medical record abstracters who regularly visit all of the major hospitals in each city and out of city in Nagasaki Prefecture. The hospitals visited include 7 of the 8 large hospitals with 300 or more beds in Hiroshima and 4 of the 5 large hospitals in Nagasaki. The 2 large hospitals that are not visited specialize in the treatment of elderly noncancer chronic disease patients. Of the 17 hospitals with 100-299 beds in the two cities, 10 are visited because of the large number of cancer patients admitted; in addition, 13 hospitals with less than 100 beds are also visited. Medical facilities with less than 20 beds, known as clinics, are not visited for case-finding. It is believed that cancer patients seen at clinics and small or medium-size hospitals are almost always referred to large institutions for complete diagnostic workup and treatment. However, the ascertainment of cases from clinics and small or medium hospitals is an important issue. Ascertainment of cases from these facilities relies on several methods: notification by physicians, death certificates, the tissue registries and physician notification. The adequacy of these methods is discussed later.

No single data source is sufficient to ensure complete case ascertainment: therefore, several sources are used within a hospital. These sources include hospital, pathology and clinical laboratory records. If a hospital has a centralized medical record system, it is used to search for relevant tumor cases. If not, as is frequently the case in Japan, the abstracters examine medical records from all relevant departments and services at each hospital. Since diagnostic indices are usually not available. abstracters review all the medical records and other documents for case-finding.

Tissue Registries

In the early 1970s specialized pathology registries were also established in Hiroshima and Nagasaki to collect and store pathological specimens and reports (Table I). These registries were initiated to facilitate studies based on tissue specimens. with the aim of improving the quality of tumor information for a population broader than that targeted by the city-based tumor registries. In 1973, the Hiroshima Prefectural Tumor Registry (referred to as the Hiroshima Tissue Registry) was established and administered by the Hiroshima Prefectural Medical Association. A total of 47 medical institutions in the prefecture currently participate in the Hiroshima Tissue Registry. The Clinical Laboratory, administered by the City Medical Association, which provides services to all practicing physicians, clinics and hospitals in the area, also reports tumor cases diagnosed on the basis of cytology or histopathology to the Tissue Registry. Many of the large institutions are visited regularly by the Registry staff for collection of materials. Others send materials by mail to the Registry. The Registry also receives reports on autopsied cases.

All diagnoses of benign or malignant tumors (including hematological neoplasms) (ICD-O codes 140-199, behavior codes 0–9) are reportable. For each biopsied or surgical case, copies of the pathology examination request form and the pathology report form are submitted along with a tissue specimen representative of the tumor. For each case of leukemia or other hematopoietic neoplasm. a standardized form developed for registration of leukemia and related conditions is submitted together with a peripheral or bone marrow blood specimen. Diagnoses of solid tumors are verified by Registry pathologists who review reports as well as tissue slides. Diagnoses of hematological neoplasms are verified by a hematologist.

A similar registry was established in Nagasaki in 1974. and tissue materials from 1973 were collected retroactively. The Nagasaki Tissue Registry is administered by the City Medical Association. The geographic area covered includes the city of Nagasaki, the three adjacent cities and their suburbs.

Tumor cases accessed by the tissue registries are referred to the Hiroshima and Nagasaki Tumor Registries for inclusion in the registries or updating of registered cases. Through the tissue registries. Hiroshima or Nagasaki residents hospitalized outside of the cities can be identified. Tissue registry material is available for 33% of the LSS cases in the tumor registry. For 2.3% of the cases. the tissue registries are the only source of case ascertainment. Thus they not only provide materials for pathology review, but serve as a case-finding data source for the LSS.

Nagasaki Prefectural Cancer Registry

In 1985, the Nagasaki Prefectural Cancer Registry was established. It is administered by the Health Department of Nagasaki Prefecture and operated by RERF (Table I). Because this registry ascertains cancer cases throughout the prefecture, it, like the tissue registrie,. offers coverage for patients who are treated outside the city. The basic approach employed by this registry relies on notification by physicians. All physicians, hospitals and medical institutions in the area are requested by the Prefectural Health Department and local medical associations to report cancer cases on a standardized form. However, collecting information only by notification is insufficient, reducing the quality of the prefectural registry data. Currently several major hospitals outside of Nagasaki City are visited by registry abstracters. Over the last 5 years approximately 5% of the newly diagnosed LSS cases were ascertained by the prefectural registry only.

Registry of Leukemia and Related Disorders

In 1948, a registry of leukemia and other hematological tumors was established in Hiroshima and Nagasaki. Cases were ascertained retrospectively from 1946. In the early years of this registry, cases of leukemia and related disorders were identified from various sources, including death certificates, ABCC/RERF clinical records, autopsy and surgical pathology records. tumor registries and newspaper reports *(26)*. In recent years, essentially all case detection is done through the tumor and tissue registries and death certificates. The Leukemia Registry is used as a supplemental source of information, especially the detailed diagnostic data. Until now, virtually all LSS reports on leukemia have been based on cases from this registry *(27)*.

Physician Notification

All physicians in the cities of Hiroshima and Nagasaki are also requested, by the medical association in each city, to report tumor cases to the city tumor registry. This passive method of case ascertainment identifies only a small proportion (less than 1%) of cases, but does provide other supplemental data.

Death Certificates

The RERF routinely obtains vital status information as part of its regular LSS mortality follow-up *(28)*. Causes of death and date of death are obtained from vital statistics death schedules. Ascertainment of deaths is believed to be essentially complete for residents of Japan *(29)*. Death certificate information is reviewed regularly and tumor cases not yet included in the tumor registries are added. About 12.6% of the LSS cases are accessed by death certificates alone. Death certificate data are also used to determine vital status for LSS tumor registry patients so that survival can be evaluated. Although there are substantial errors in detection of certain cancer sites using death certificate diagnoses *(1, 2, 30, 31)*. there is no evidence that inaccuracies are related to atomic bomb exposure or individual dose estimates (32).

Other RERF Records

The ABCC surgical pathology program was started in 1949 in Hiroshima and 1950 in Nagasaki and ended in 1973. As part of this program surgical specimens for tumor and nontumor cases were submitted by physicians, clinics and hospitals in the Hiroshima and Nagasaki area. Postmortem examinations of members of the LSS sample were conducted during the 1960s and 1970s as a priority program of ABCC/RERF *(33)*. The autopsy rates ranged from 30 to 40% in the 1960s but declined to about 10% by the late 1970s. The program was terminated in 1988 *(1,* 33). Diagnoses made based on these autopsies are another useful source of case ascertainment *(33)*, but these account for a very small proportion of the cases.

The AHS includes a subsample of approximately 20,000 members of the LSS cohort, weighted toward high doses. who are invited to participate in regular biannual c1inical examinations at RERF. A great deal of clinical information is collected on these people, including information on past and present tumors. Relevant data are added to the Tumor Registry database.

RECORD ABSTRACTION

At the time of hospital visit, pertinent personal and medical information is extracted from hospital records onto a standard abstraction form. It includes: *(1)* patient identification data; *(2)* hospital and physician identification data; *(3)* hospitalization and referral history relevant to the current illness; *(4)* admission and discharge dates; *(5)* clinical diagnosis: *(6)* histological diagnosis; *(7)* cytological diagnosis; *(8)* surgical diagnosis and findings; *(9)* findings from other diagnostic procedures, i.e., radiological, endoscopic, immunological and other; *(10)* tumor treatment modalities, i.e., surgical, radiation, chemotherapy, hormone and other; and *(11)* vital status, Abstract forms are reviewed and coded at the Hiroshima and Nagasaki RERF (offices, Data abstraction follows the detailed data collection and coding rules describcd in the RERF Data Acquisition Manual. This manual, a modified version of one used by the SEER program *(19)*, is used under the guidance of the registry physicians and pathologists. Cases included in the tumor registries adhere strictly to the Data Acquisition Manual rules for case definition.

Record abstractors are well trained having received in-house training and completed a formal course given for tumor registries at the National Cancer Center. The SEER *(34)* training manuals were translated into Japanese, and these manuals, adapted to local record-keeping practices, are now in use for ongoing in-house staff training and to train new staff.

RECORD REVIEW

To achieve consistency in case ascertainment and data handling, coders and abstracters from both cities meet regularly to review all new LSS cases. Information on each case is reviewed independently by at least two coders and, in addition. in-house meetings are held to discuss "difficult cases." Especially difficult cases are referred to the tumor registry pathologists and physicians. Decisions made are kept on file for use in dealing with future cases. Original documents are kept in individual patient files to facilitate further record review if needed. After the final record review, a summary data record is constructed.

Since tumor notification can come from more than one source, the data are also checked, manually and by computer, to eliminate duplicate registrations. All cases with possible multiple primary tumors are reviewed. The definitions and rules used to determine independent primary tumors follow those employed by the SEER program *(19).*

DATA ENTRY AND EDITING

Data are entered into a database on the RERF mainframe computer. All potentially eligible cases are entered into the computerized database. Until a final decision on acceptance or rejection is made, cases are coded as "pending." Cases later found ineligible are coded as rejected, but kept in the database. All newly accessed information is checked against accepted, pending and rejected cases for updating the database.

Data are subjected to manual and computerized edit checks. These include checks for valid codes, for between-item consistency and for unlikely but valid conditions. In addition to simple checks for legitimate codes for specific variables, consistency checks are also done using various algorithms including site-morphology checks based on ICD-O codes. The error rate detected by computerized edit checks ranges from 3 to 4% each month.

DATA QUALITY

Completeness, accuracy or validity, and timeliness are considered essential for optimal data quality *(35,* 36). The International Agency for Research on Cancer (IARC) uses three numerical indices as measures of data quality for its cancer registry reporting project *(17):* (1) the proportion of cases registered with a microscopically (or histologically) verified diagnosis (histological verification, HV): (2) the proportion of cases registered from death certificates only (DCO): and (3) the mortality/incidence ratio (M/I). This ratio provides a gauge of completeness of case ascertainment, whereas the number of histological verifications is a measure of accuracy. The definition of DCO is unclear. Some registries, including Hiroshima and Nagasaki, define DCO cases as those which were ascertained by death certificate only, even though additional medical data were obtained subsequently from other sources. Using this definition, DCO is a measure of completeness of case ascertainment. In contrast, other registries define DCO as cases for which information comes from death certificates only; i.e., no clinical data were obtained on follow-back (confirmation of data). The DCO rate based on this definition is an indicator of accuracy. Since Hiroshima and Nagasaki employ the first definition of DCO, it is used as a measure of completeness in this report.

Completeness measures the proportion of cases in the target population identified by the registry. Although adequate evaluation of completeness of ascertainment is difficult, useful indicators are available *(36).* The DCO rate indicates the minimum proportion of cancer cases missed by the Registry through its regular case ascertainment system. A high DCO rate indicates that a large number of fatal cancers were not identified by the registry and suggests that other nonfatal cancers were also overlooked. The reliability of DCO information depends on the accuracy of death certificate diagnoses. Another index of completeness is the M/I ratio. If the number of reported cancer deaths is larger than the number of incident cases. then either there is substantial underreporting in the cancer registry or there are a large number of false-positive death certificate diagnoses.

Another important element in data quality is accuracy *(35).* One quantitative measure frequently used to evaluate accuracy of cancer diagnosis is the proportion of HV cases. because at the very least, these diagnoses were based on a microscopic examination of some of the tumor tissue. With the exception of a few sites for which other diagnostic methods are equally reliable, the higher the proportion of HV cases, the more accurate the diagnosis. It should be noted, however. that the HV rate varies considerably by tumor site. The HV rate for all sites combined is influenced by the distribution of sites. There is also variability in classifying neoplasms ameng pathologists.

The proportion of individual data items which are recorded completely and correctly is another index of accuracy. To check this type of accuracy, monitoring of "unknowns" is recommended. For each registry, IARC reports the number of cases with unknown age and primary site *(18).*

Population-based Tumor Registry Data

While the primary aim of this paper is to examine the quality of the LSS cohort-based tumor registry data, it is also pertinent to report on the quality of the population-based tumor registries in the two cities from which the LSS incidence data are derived.

[b]Percentage of cases notified from a death certificate only.
[c]Percentage of cases verified histologically.
[d]Ratio of mortality to incidence.

Completeness. Currently, the Hiroshima and Nagasaki tumor registries show DCO rates of 7–9%, which are better than any in Japan and comparable to those for many other established registries (Table II). Studies at RERF of the overall accuracy of the underlying cause of death reported on death certificates compared with autopsy findings have shown that the cancer detection rate (probability of a death certificate correctly identifying cancer diagnosed at autopsy as the cause of death) was about 80%, while the confirmation rate (probability of a death certificate being correct in listing cancer diagnosed at autopsy as the cause of death) is about 90% *(9, 32)*. These figures are similar to those found in other countries *(37)*. Since the tumor registries screen for any mention of cancer (not only underlying cause of death) on death certificates, the actual detection rates would be higher and the confirmation rates lower than the above figures. Thus inclusion of DCO cases increases case ascertainment at the cost of an increase in false-positive diagnoses. Death certificate detection and confirmation rates vary widely depending on site, place of death (home, hospital, etc.), age at death and year of death *(1)*. Results of a study of a random sample of 392 DCO cases from 1985 in the Osaka Tumor Registry are reassuring since the number of false positives was small. In this study additional information could be found on 346 cases. Of these, all but 1 actually had cancer on review of the medical records *(18)*. It should be noted, however. that these findings refer to any cancer. and that the death certificate accuracy rate for any specific cancer site is probably not so high.

The overall M/I ratios for the Hiroshima and Nagasaki Tumor Registries are about 0.5 and comparable to those reported from other registries (Table II). An evaluation of the M/I ratios by site for the Hiroshima and Nagasaki Registries revealed ratios in excess of one for cancers of the small intestine, liver, pancreas. male breast. uterus NOS. other endocrine organs and primary site uncertain. For cancers of

TABLE III
Indices of Quality by Age and Time, LSS Solid Cancer Cases

Time/Age	Number of cases	DCO (%)	M/I	HV (%)
1958–1959	427	22.2	0.70	53.6
<65 years	245	11.8	0.59	66.5
≥65 years	182	16.4	0.84	36.3
1960–1969	2,566	11.3	0.65	75.5
<65 years	1,226	7.1	0.59	80.9
≥65 years	1,340	15.1	0.70	70.6
1970–1979	2,929	12.1	0.67	75.9
<65 years	1,065	6.1	0.55	84.9
≥65 years	1,864	15.5	0.75	70.8
1980–1987	2,691	12.9	0.63	78.1
<65 years	1,045	7.8	0.46	85.9
≥65 years	1,646	16.2	0.73	73.2
All years	8,613	12.6	0.65	75.4
<65 years	3,581	7.3	0.54	82.6
≥65 years	5,032	16.4	0.73	70.3

the liver, pancreas, uterus NOS and primary site uncertain, the same pattern was seen in most American and European registries (18). Since these sites are known to have very low confirmation rates (34, 56, 13 and 0%, respectively) when compared to autopsy diagnoses (1), a high M/I ratio would be expected. The high M/I ratio for uterus NOS and the low M/I ratio for uterine cervix suggest that many deaths reported to be from uterus NOS include deaths from uterine cervix. The number of incident cases of small intestine, male breast and other endocrine cancers were so small that the M/I ratios were uninterpretable. For sites with poor survival the M/I ratio should be fairly close to 1. The M/I ratios for male lung cancer were 0.95 and 0.74 for Hiroshima and Nagasaki, respectively which were similar to the ratios seen in other registries. In contrast, M/I ratios were less than 0.20 for skin and thyroid cancer, reflecting the very low fatality rate of these cancers,

In an attempt to determine the number of cases missed by not including all hospitals in the systematic hospital search program, a pilot study of three medium-size hospitals in the Hiroshima area was conducted. For the period 1980–1987, 120 reportable LSS cases were identified. Of these, only 4 (3%) had not been accessed in the tumor registry. Since These three hospitals together have 790 beds and there are another 25 medium-size hospitals with a total of 3,500 beds, approximately 18 missed cases might be expected. Since about 2,700 LSS cases with cancer were registered in the Hiroshima Tumor Registry from 1980 to 1987, the estimated 18 missed cases represent about 0.7% of the total cancers. This is likely to be an overestimate of the number of missed cases because the above three hospitals are known to admit more cancer patients than others of equal size and smaller hospitals are more likely to make referrals.

While none of the completeness assessments are sufficient to evaluate the adequacy of case identification individually, together they provide an indication that the level of ascertainment is high. Efforts to assess and improve case ascertainment through special evaluation studies and programs to incorporate the medium-size hospitals into the registry system are described later.

Accuracy. The Hiroshima and Nagasaki Tumor Registries have HV rates of 67–84%, which are among the highest in Japan and are comparable to those at established registries in other countries (Table II). The percentage of persons of unknown age is very small for all registries including Hiroshima and Nagasaki, and the percentage of unknown primary sites is lower in Hiroshima and Nagasaki than in many other registries.

Timeliness. Timeliness of reporting is another requisite for a good tumor registry. The accession of cases by the Nagasaki Tumor Registry is undertaken on an annual basis: each hospital is visited every year and all the medical records for the previous year's admissions are abstracted. With the resumption of routine hospital case-finding in Hiroshima, the Hiroshima Tumor Registry's accession is now complete through 1987 and most of the 1988–1989 cases have been ascertained. Once case ascertainment is complete for Hiroshima. accession of cases will be undertaken annually as in Nagasaki,

LSS Tumor Registry Data

Completeness. The DCO rate for the 8,613 first primary tumors included in the LSS tumor registry report *(14)* was 12.6%. This was larger than in most North American registries and somewhat higher than for the general populations of Hiroshima (8%) and Nagasaki (7%), mainly because the LSS sample includes a substantial proportion of elderly people and the LSS registry includes death certificate information for people who have moved out of the tumor registry catchment areas. As indicated earlier, in the Hiroshima and Nagasaki registries, DCO cases are defined as those identified by death certificate only, whereas in some registries DCO is defined as cases registered solely on the basis of death certificates. This difference in definition can alter the DCO rates considerably. Differences in DCO rates by age at death were striking: for persons who died after age 65, 16.4% were detected by DCO, whereas for those less than 65 years old, only 7.3% were DCO cases (Table III). Similar differences by age were also noted for the M/I ratio. An examination by time showed little or no change in DCO rates or M/I ratios over time.

Table IV shows the DCO rate and M/I ratio by cancer site in the LSS. Cancers of the oral cavity, nasal cavity, larynx, nonmelanoma skin, breast, uterine cervix and corpus, bladder and thyroid all had DCO rates of less than 5%. High DCO rates were seen for cancers of the liver. pancreas, lung and uterus NOS. The M/I ratios were relatively low for most

TABLE IV
Indices of Quality by Cancer Site, LSS Solid Cancer Cases

Cancer site	Number of cases	DCO (%)	M/I	HV (%)
Oral cavity	132	4.5	0.50	92.4
Esophagus	185	10.3	0.96	71.9
Stomach	2,658	14.1	0.70	72.8
Colon	457	9.2	0.53	80.7
Rectum	351	10.5	0.65	82.3
Liver	585	32.8	1.05	38.8
Gallbladder	295	12.2	0.61	70.5
Pancreas	240	17.1	0.91	55.0
Nasal	55	0	0.75	85.5
Larynx	80	3.8	0.50	90.0
Lung	872	18.3	0.85	69.4
Nonmelanoma skin	168	2.5	0.14	96.4
Breast (female)	529	1.9	0.27	95.1
Uterine cervix	553	0.9	0.16	96.7
Uterine corpus	85	1.2	0.16	97.6
Uterus NOS	86	29.1	2.48	55.8
Ovary	133	6.0	0.62	84.2
Prostate	140	7.1	0.45	85.7
Bladder	210	4.8	0.41	82.9
Kidney	73	9.6	0.55	76.7
Nervous system	125	10.4	0.43	79.2
Thyroid	225	3.1	0.20	93.3

of the sites with low DCO rates except for the nasal cavity. The M/I ratios were especially low for nonmelanoma skin, uterine cervix and corpus, and thyroid. Neither the DCO rate nor the M/I ratio examined by radiation dose revealed statistically significant differences (Table V).

For a further assessment of completeness of case-finding, a number of case ascertainment evaluations were undertaken. While the ascertainment of tumor casts for the tumor registry relies heavily on case-finding at medium- and large-size hospitals, it is believed that many cases that are first recognized at small hospitals or clinics are referred to larger hospitals. For the period of 1958-1987, 36.4% of LSS cancer cases were first admitted to small hospitals (20-99 beds) or

TABLE V
Measures of Data Quality by Radiation Dose, LSS Solid Cancer Cases

Radiation dose (kerma, Gy)	Number of cases	DCO (%)	M/I	HV (%)
Less than 0.01	3,910	13.0	0.66	74.3
0.01–0.99	4,184	12.6	0.66	76.2
≥1	519	10.0	0.61	77.1

clinics (<20 beds), 17.2% to medium-size hospitals (100-299 beds), and 46.4% to large hospitals (>=300 beds). The distribution of cases by the size of hospitals at which patients were first seen did not differ by dose (Table VI). suggesting no preferential admission of exposed over nonexposed patients to large hospitals.

An additional check on the completeness of the tumor registries was done as part of two site-specific LSS incidence studies. In a study of colon cancer *(11)*, special efforts were made to ascertain cases not already identified through the tumor registries. An additional 2 cases were found, both from an institution which was not accessible to the tumor registry medical abstracters at that time. Since then, this institution has agreed to participate in the registry. Medical abstraction of all records, past and present, is currently under way. Cases included in a breast cancer study *(7)* were also compared to those found in the tumor registry. Out of 529 cases, 14 (2.6%) were identified through the breast cancer study only (M. Tokunaga and K. Mabuchi, personal communication).

As part of an LSS study on leukemia and other hematopoietic tumors *(15)*. the Tumor Registry and Leukemia Registry were compared. After a preliminary review of the registry records, 4.6% of the Tumor Registry lymphoma cases and none of the leukemia cases were rejected. Out of a total of 286 lymphomas, 278 (97.2%) were ascertained by the Tumor Registry. For leukemias, 93.0% (186/200) were identified by the Tumor Registry.

TABLE VI
Distribution of LSS Solid Cancer Cases by Size of Hospital Providing First Diagnosis and Radiation Dose

	Radiation dose (kerma, Gy)					
	0–0.01		0.01–0.99		>1.0	
Hospital size	Number	Percentage	Number	Percentage	Number	Percentage
Large (≥300 beds)	1,856	47.5	1,907	45.6	230	44.3
Medium (100–299 beds)	626	16.0	767	18.3	92	17.7
Small (20–99 beds)	171	4.4	146	3.5	14	2.7
Clinic (<20 beds)	1,257	32.1	1,364	32.6	183	35.3
Total	3,910	100	4,184	100	519	100

TABLE VII
Number of Data Sources Used to Ascertain Cancer by Cancer Site, LSS Solid Cancer Cases

		Number of data sources			
Cancer site	Number of cases	1	2	3	4+
All sites	8,613	19.9	43.1	29.4	7.5
Oral cavity and pharynx	185	12.9	41.7	40.9	4.5
Digestive system	4,797	20.5	42.8	29.3	7.5
Respiratory system	1,027	18.0	42.1	30.7	9.2
Skin	181	20.4	47.0	29.3	3.3
Female breast	529	22.5	38.9	29.7	8.9
Female genital organs	891	18.2	46.1	28.7	7.0
Male genital organs	160	11.9	45.0	35.6	7.5
Urinary system	325	14.1	42.8	32.6	10.5
Nervous system	125	24.0	52.8	20.0	3.2
Thyroid	225	20.9	45.8	28.9	4.4
Other and ill-defined sites	221	32.1	41.2	21.7	5.0

[redacted]

Accuracy. In both Hiroshima and Nagasaki HV excludes diagnoses based on cytology only, but for leukemia includes diagnoses based on peripheral blood. The overall rate of HV was 75.4%, but the rates improved slightly over time, and were higher for persons under 65 years of age than for those over 65 (Table III). The rate of HV varied considerably by site (Table IV) and for liver cancer was as low as 38.8%, but it was higher than 90% for oral cavity, larynx, nonmelanoma skin, female breast, uterine cervix and corpus, and thyroid cancer. By dose group, the rate of HV was 74.3% for the nonexposed compared to 76.2 and 77.1% for those exposed to 0.01–0.99 Gy and >1 Gy, respectively (Table V). The differences are not statistically significant.

As part of a special study on skin cancer in progress (38), a pathology review of the cases was conducted. A comparison of a sample of 60 tumor registry diagnoses and diagnoses after record review by a pathologist revealed one tumor coded correctly as squamous cell carcinoma of the lip (ICD-O 140.1) in the tumor registry, whereas the pathologist coded this tumor as a skin cancer (ICD-O 173.0). In addition, two skin tumors classified as squamous cell carcinoma in the registry were classified differently by the pathologist: one as Bowen's disease and the other as basal cell carcinoma. Thus there was a difference of 1.7% based on the topography codes and 3.3% for the morphology codes.

TABLE VIII
Primary Source of Case Ascertainment, LSS Solid Cancer Cases

Best information available	Number	Percentage
Medical record abstracts	6,059	70.3
Tissue registry data	505	5.9
Autopsy	309	3.6
Autopsy only	315	3.7
Other, excluding DCO	339	3.9
DCO	1,086	12.6
Total	8,613	100

TABLE IX
Primary Source of Case Ascertainment by Radiation Dose, LSS Solid Cancer Cases

	Radiation dose (kerma, Gy)					
	Less than 0.01		0.01–0.99		1+	
	Number	Percentage	Number	Percentage	Number	Percentage
Medical record abstracts	2,800	71.6	2,891	69.1	368	70.9
Tissue registry data	200	5.1	271	6.5	34	6.6
Autopsy	133	3.4	161	3.8	15	2.9
Autopsy only	125	3.2	172	4.1	18	3.5
DCO or other	652	16.7	689	16.5	84	16.2
Total	3,910	100	4,184	100	519	100

DISCUSSION

As judged by the conventional measures of data quality, i.e., DCO rate, M/I ratio and the rate of HV, the quality of the Hiroshima and Nagasaki Tumor Registries was considered superior to other population-based registries in Japan and comparable to good registries in other parts of the world. Skeet suggested that the maximum tolerable error rates be 5% for the three-digit ICD-O codes and 0.5% for sex *(36)*. The Hiroshima and Nagasaki registries have error rates below these levels. These standard measures of data quality were used in accordance with the recommendations by the International Association of Cancer Registries *(17, 39)*. They are by no means a perfect way of measuring completeness and accuracy, but should be looked at together to give a judgment of the overall quality. Special studies and monitoring programs undertaken in recent years tend to strengthen the positive impression gathered by evaluation of the conventional quality-control indices. While some cases must be missed because some small and medium-size hospitals are not visited regularly for case-finding, the results of a pilot survey suggest that the number is extremely small. Many patients initially treated at small or medium-size hospitals are later referred to large hospitals. For other patients alternative methods such as tissue registries or physician notification seem effective in identifying cases.

Although the LSS tumor incidence data arc derived largely from the population-based registries in Hiroshima and Nagasaki. these registries supplement their routine case-finding procedures with additional data from the RERF pathology and clinical programs for LSS members. When data from multiple sources are used, an obvious concern is the lack of uniformity in the resulting incidence data that may have undesirable effects on cancer risk estimation. The homogeneity of incidence data across various substrata, such as by age, time and radiation dose, was analyzed using both conventional and specific measures of data quality developed for the LSS data set. The analysis revealed no indication of the presence of potential bias or confounding which may affect cancer risk estimates using the present data set.

The DCO rate and rate of HV were not statistically significantly correlated with radiation dose. Although statistically insignificant, the DCO rate was slightly lower and the rate of HV slightly higher in high-dose than in low-dose groups (Table V). This can be explained at least in part by the increased incidence of certain cancer sites in high-dose groups, such as breast, skin and thyroid, sites which have very low DCC) rates and very high rates of HV. The proportion of cases with detailed medical record data or pathology-based diagnoses also was not correlated with radiation dose. Patients first diagnosed at hospitals and clinics of various sizes were equally represented in low-, medium- and high-dose groups.

Concern has been expressed over the possibility of a bias by including cases ascertainable from the autopsy program. Since many of the tumor cases were also identified from other sources including: medical records and death certificates. The number of cases that were identificd by autopsies only was rather small and accounted for only 3.7% of all cases. Because the autopsy program was especially active between 1960-1969, the rate increased to 8.4% during this decade. However, it is unlikely that this would influence risk estimates because no differences were found in the percentage of autopsy-only cases by dose. It also should be remembered that the solid tumor cases included in the present series excluded “occult" or "latent"- carcinomas detected at autopsy.

Despite the fact that the quality of data in the Hiroshima and Nagasaki Tumor Registries appears to be comparable to many other registries in the world, they have not yet reached the level of the SEER registries or some of the well-established European registries. Although work is continuing to improve data quality, some problems that are inherent to the Japanese medical system make this difficult. The percentage of cases having histology or cytology is lower in Japan than in many other countries: thus case ascertainment based on

TABLE X
Components of a Quality Control Program

Objective	Method	Importance	RERF
Standardize and define reportable cases	Written documentation of definitions	ESSENTIAL	*Yes*
	Review of questionable records	ESSENTIAL	*Yes*
	Use of test cases	Desirable	No
Define data items	Data acquisition manual	ESSENTIAL	*Yes*
	Periodic review of items	Desirable	*Yes*
Asscss completeness of case-finding	List of sources	ESSENTIAL	*Yes*
	Documentation of case-finding procedures	ESSENTIAL	*Yes*
	Active check on outside sources	Very desirable	*Yes*
	Formal case-finding study	Desirable	Informal
Assess completeness of data capture	Monitoring of "Unknowns"	Very desirable	*Yes*
	Monitoring capture of therapy information	Very desirable	NA
Control timeliness	Monitoring of number of cases "on time"	ESSENTIAL	Informal
	Standards for registration and follow-up rates	Very desirable	Informal
Assess accuracy,	Edit checks manual/computerized	ESSENTIAL	*Yes*
	Review of abstract/coding by supervisor	ESSENTIAL	*Yes*
	Systematic re-abstracting of routine cases	Very desirable	Informal
	Systematic re-abstracting of special cases	Desirable	Informal
Provide training	Orderly training of new staff members	ESSENTIAL	*Yes*
	In[rti-institutional workshops	Very desirable	*Yes*
	Written documentation of unusual cases	Very desirable	*Yes*
	Formal continuing education	Desirable	*Yes*

pathology reports has some limitations. The lack of diagnostic indices and hospital tumor registries also hinders case-finding. The plethora of small hospitals and clinics further complicates case ascertainment, although our analyses suggest that most cancer patients at small hospitals or clinics are referred to larger hospitals from which they are reported to the registry. In fact, 39% of the tumor cases analyzed in the LSS tumor registry report were first treated in clinics or small hospitals.

Hilsenbeck *et al. (35)* summarized the components of a good data quality control program. In Table X, the RERF data quality program is shown in relation to their suggested criteria. All "essential" elements of their approach have been formally incorporated into the RERF program. Other than the use of test cases, all other components of the quality control program are also done at RERF, although some of them are not formalized.

The Hiroshima and Nagasaki Tumor Registries made tremendous efforts to ensure data consistency. To do this. various operational and training manuals were developed and old data were reviewed. This standardization was helpful in evaluating the LSS tumor incidence data. It should, however, be noted that because of the strict case definition used by the tumor registries, the cases included in registry-based studies may differ somewhat from cases used in previous site-specific studies.

Currently and over the next few years, several site-specific cancer incidence studies are being conducted. It is expected that these studies will help assess and possibly also improve case finding. Since errors are frequently discovered during the course of using data, the more they are exploited the better they will become *(40)*. As noted by Muir and Waterhouse *(41)*. "The only perfect data are, after all, those that are never used."

APPENDIX

Current members of the tumor and tissue registry committees are listed below:

Hiroshima City Medical Association Tumor Statistics Committee

Yukio Ochikubo (Hiroshima City Medical Association)
Akio Orimen (Hiroshima City Medical Association)
Takayuki Chabata (Hiroshima City Medical Association)
Kanshu Nagashima (Hiroshima City Medical Association)
Yasuji Yamamoto (Hiroshima City Medical Association)
Yukiharu Sasaki (Hiroshima City Medical Association)
Takashi Takiguchi (Hiroshima City Medical Association)
Chikako Ito (Hiroshima A-bomb Survivors Health Management Center)
Toshiyuki Fukuhara (Prefectural Hiroshima Hospital)

Tetsuo Monzen (Ken-Ei-Ren)
Tsutomu Yamamoto (Hiroshima Prefectural Medical Association)
Hiromasa Sasaki (Hiroshima NTT Hospital)
Tadayoshi Rikita (Hiroshima JR Hospital)
Shiro Nakai (Hiroshima Memorial Hospital)
Koso Mitsuba (Chuden Hospital)
Toyomichi Nakano (Mazda Hospital)
Suminori Akiba (RERF)
Kiyohiko Mabuchi (RERF)

Nagasaki City Medical Association Tumor Statistics Committee

Masayuki Terasaki (Nagasaki City Medical Association)
Ryozo Shukuwa (Nagasaki City Medical Association)
Katsuaki Joya (Nagasaki City Medical Association)
Shigenobu Miyagi (Nagasaki City Medical Association)
Yoneichi Harada (Nagasaki City Medical Association)
Hiroshi Fujii (Nagasaki City Medical Association)
Katsuyo Shirahige (Nagasaki City Medical Association)
Kinichiro Hamasato (Nagasaki City Medical Association)
Toru Yamabe (Nagasaki University School of Medicine)
Takayuki Kanematsu (Nagasaki University School of Medicine)
Masao Tomita (Nagasaki University School of Medicine)
Toshiaki Usui (Nagasaki University School of Medicine)
Yoshiro Tsuji (Nagasaki University School of Medicine)
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Takayoshi Ikeda (Nagasaki University School of Medicine)
Takashi Taguchi (Nagasaki University School of Medicine)
Ichiro Sekine (Nagasaki University School of Medicine)
Yutaka Okumura (Nagasaki University School of Medicine)
Kuniaki Hayashi (Nagasaki University School of Medicine)
Tadashi Egawa (Nagasaki Municipal Hospital)
Takeshi Ishizaki (Nagasaki Municipal Hospital Adult Disease Center)
Hideaki Mukai (Nagasaki Atomic Bomb Hospital)
Soroku Saeki (National Clinical Nagasaki Hospital)
Tomohiko Mukasa (Mitsubishi Hospital)
Chuichiro Takagi (Juzenkai Hospital)
Sunao Fukui (Nagasaki Memorial Hospital)
Makoto Ishino (Nagasaki Prefectural Office)
Iwao Babasaki (Nagasaki City Central Public Health Center)
Omimasa Imamura (Nagasaki Prefectural Medical Association)
Michito Ichimaru (Saseho Municipal Hospital)
Katsutaro Shimaoka (RERF)
Midori Soda (RERF)

Hiroshima Prefectural Medical Association Tumor Registry Steering Committee

Kouki Inai (Hiroshima University School of Medicine)
Tokuo Tsubokura (Hiroshima University School of Medicine)
Nanao Kamada (Hiroshima University Geniken)
Eiichi Tahara (Hiroshima University School of Medicine)
Koji Nanba (Hiroshima University. Faculty of Integrated Arts and Sciences)
Norihiko Hayakawa (Hiroshima University Geniken)
Tetsuo Monzen (Ken-Ei-Ren)
Tsutomu Yamamoto (Hiroshima Prefectural Tumor Registry Office)
Tadanori Hiramoto (Hiroshima Citizen Hospital)
Tsukasa Okamoto (National Fukuyama Hospital)
Yuzo Hayashi (Asa Shimin Hospital)
Shoichi Katayama (National Kure Hospital)
Toshiyuki Fukuhara (Prefectural Hiroshima Hospital)
Hisao Ito (Hiroshima University School of Medicine)
Megumu Fujihara (Hiroshima Red Cross Hospital)
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